

We Claim:

1. A microparticle having an adsorbent surface, said microparticle comprising:  
a polymer selected from the group consisting of a poly( $\alpha$ -hydroxy acid), a  
5 polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a  
polycyanoacrylate; and  
a detergent.
2. The microparticle of claim 1, further comprising a first biologically active  
10 macromolecule adsorbed on the surface thereof, wherein the first biologically active  
macromolecule is at least one member selected from the group consisting of a polypeptide, a  
polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a  
transcription or translation mediator, an intermediate in a metabolic pathway, an  
immunomodulator, and an adjuvant.
- 15 3. The microparticle of claim 2, further comprising a second biologically active  
macromolecule encapsulated within said microparticle, wherein the second biologically active  
macromolecule is at least one member selected from the group consisting of a polypeptide, a  
polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a  
20 transcription or translation mediator, an intermediate in a metabolic pathway, an  
immunomodulator, and an adjuvant.
4. The microparticle of any of claims 1-3, wherein the microparticle comprises a  
poly( $\alpha$ -hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide)  
25 and poly(D,L-lactide-co-glycolide).
5. The microparticle of any of claims 1-4, wherein the microparticle comprises  
poly(D,L-lactide-co-glycolide).

6. The microparticle of any of claims 1-5, wherein the detergent is a cationic detergent.

5 7. The microparticle of any of claims 1-5, wherein the detergent is an anionic detergent.

8. The microparticle of any of claims 1-5, wherein the detergent is a nonionic detergent.

10 9. The microparticle of any of claims 2-8, wherein the first biologically active macromolecule is an antigen selected from the group consisting of gp120, p24gag, p55gag, and Influenza A hemagglutinin antigen.

15 10. The microparticle of any of claims 2-9, wherein the first biologically active macromolecule is a polynucleotide which encodes gp120.

11. The microparticle of any of claims 3-10, wherein the second biologically active macromolecule is an adjuvant.

20 12. The microparticle of any of claims 1-11, wherein the adjuvant is an aluminum salt.

25 13. A microparticle composition comprising a microparticle of any of claims 1-12 and a pharmaceutically acceptable excipient.

14. A microparticle composition comprising a microparticle according to any of claims 1-13, further comprising an adjuvant.

30 15. A microparticle composition of claim 14, wherein the adjuvant is a member selected from the group consisting of CpG oligonucleotides, LTK63, LTR72, MPL, and an aluminum salt.

16. A microparticle composition of claim 15, wherein the adjuvant is an aluminum salt which is aluminum phosphate.

5        17. A method of producing a microparticle having an adsorbent surface, said method comprising the steps of:

- (a) dispersing a mixture of a polymer solution and a detergent, wherein the polymer solution comprises a polymer selected from the group consisting of a poly( $\alpha$ -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and  
10 a polycyanoacrylate, wherein the polymer is present at a concentration of about 1% to about 30% in an organic solvent, and wherein the detergent is present in the mixture at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1; and  
(b) removing the organic solvent from the emulsion.

15        18. The method of claim 17 wherein the detergent is an anionic detergent.

19. The method of claim 17 wherein the detergent is a cationic detergent.

20. The method of claim 17 wherein the detergent is a nonionic detergent.

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21. The method of any of claims 17-20 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.0001:1 to about 0.01:1.

22. The method of any of claims 17-20 wherein the detergent is present at a weight to  
25 weight detergent to polymer ratio of from about 0.001:1 to about 0.01:1.

23. The method of any of claims 17-20 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.005:1 to about 0.01:1.

24. The method of any of claims 17-23, wherein the microparticle comprises a poly( $\alpha$ -hydroxy acid) selected from the group consisting of poly(L-lactide), poly(D,L-lactide) and poly(D,L-lactide-co-glycolide).

5        25. The method of claim 24, wherein the microparticle comprises poly(D,L-lactide-co-glycolide).

26. The method of claim 25, wherein the microparticle comprises poly(D,L-lactide-co-glycolide) present at a concentration of about 3% to about 10%.

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27. A method of producing a microparticle having an adsorbent surface to which a biologically active macromolecule has been adsorbed, said method comprising the steps of:

15        (a) emulsifying a mixture of a polymer solution and a detergent to form an emulsion, wherein the polymer solution comprises a polymer selected from the group consisting of a poly( $\alpha$ -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate, wherein the polymer is present at a concentration of about 1% to about 30% in an organic solvent, and wherein the detergent is present in the mixture at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1;

20        (b) removing the organic solvent from the emulsion, to form said microparticle having the adsorbent surface; and

      (c) adsorbing the macromolecule to the surface of the microparticle.

25        28. The method of claim 27, wherein the macromolecule is at least one member selected from the group consisting of a pharmaceutical, a polynucleotide, a polynucleoside, a polypeptide, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, an antigen, and an adjuvant.

30        29. The method of any of claims 27-28, wherein the macromolecule is an antigen selected from the group consisting of gp120, p24gag, p55gag and Influenza A hemagglutinin antigen.

30. The method of claim 29, wherein the macromolecule is a polynucleotide which encodes gp120.

5 31. The method of any of claims 27-30 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.0001:1 to about 0.01:1.

32. The method of any of claims 27-30 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.001:1 to about 0.01:1.

10 33. The method of any of claims 27-30 wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.005:1 to about 0.01:1.

34. A microparticle made according to the method of any of claims 17-33.

15 35. A microparticle composition comprising a microparticle of claim 34 and a pharmaceutically acceptable excipient.

20 36. A method of producing a microparticle composition comprising a microparticle having an adsorbent surface to which a biologically active macromolecule has been adsorbed, said method comprising the steps of:

(a) emulsifying a mixture of a polymer solution and a detergent to form an emulsion, wherein the polymer solution comprises a polymer selected from the group consisting of a poly( $\alpha$ -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a polycyanoacrylate, wherein the polymer is present at a concentration of about 1% to about 30% in an organic solvent, and wherein the detergent is present at a weight to weight detergent to polymer ratio of from about 0.00001:1 to about 0.1:1;

25 (b) removing the organic solvent from the emulsion, to form said microparticle having the adsorbent surface;

30 (c) adsorbing the macromolecule to the surface of the microparticle; and

(d) combining the microparticle having the adsorbed macromolecule from step (c) with a pharmaceutically acceptable excipient to form said microparticle composition.

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37. A microparticle composition made according to the method of claim 36.

38. A method of delivering a therapeutically effective amount of a macromolecule to a vertebrate subject comprising the step of administering to the vertebrate subject a microparticle composition of any of claims 13-16, 35, or 37.

10 39. Use of a microparticle composition of any of claims 13-16, 35, or 37 for diagnosis of a disease.

40. Use of a microparticle composition of any of claims 13-16, 35, or 37 for treatment of a disease.

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41. Use of a microparticle composition of any of claims 13-16, 35, or 37 for a vaccine.

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42. Use of a microparticle composition of any of claims 13-16, 35, or 37 for raising an immune response.

43. A microparticle having an adsorbent surface, said microparticle comprising:  
a biodegradable polymer; and  
a detergent.

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44. The microparticle of claim 43, further comprising a first biologically active macromolecule adsorbed on the surface thereof, wherein the first biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

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45. The microparticle of claim 44, further comprising a second biologically active macromolecule encapsulated within said microparticle, wherein the second biologically active macromolecule is at least one member selected from the group consisting of a polypeptide, a  
5 polynucleotide, a polynucleoside, an antigen, a pharmaceutical, a hormone, an enzyme, a transcription or translation mediator, an intermediate in a metabolic pathway, an immunomodulator, and an adjuvant.

46. A microparticle composition comprising a microparticle of any of claims 44-45  
10 and a pharmaceutically acceptable excipient.

47. The microparticle composition comprising a microparticle according to claim 46, further comprising an adjuvant.

15 48. Use of a microparticle composition of any of claims 46-47 for diagnosis of a disease.

49. Use of a microparticle composition of any of claims 46-47 for treatment of a  
20 disease.

50. Use of a microparticle composition of any of claims 46-47 for a vaccine.

51. Use of a microparticle composition of any of claims 46-47 for raising an immune  
25 response.